- 1. (Currently Amended) A process for preparing a pharmaceutical composition comprising the steps of:
- (a) propagating a mutant herpes simplex virus (HSV) having a mutation in its endogenous HSV VP16 gene or a homologue thereof, which process comprises by infecting a cell line with the mutant herpes virus and culturing the cell line,

wherein the HSV has a mutation in its endogenous VP16 gene which reduces or abolishes the ability of the protein encoded by the VP16 gene to activate viral transcription without disrupting the structural activity of the protein; and

wherein the cell line comprises a nucleic acid sequence <u>from a non-HSV herpes</u> <u>virus</u> encoding a functional <u>equivalent of the herpes simplex virus</u> (HSV) VP16 polypeptide, or a homologue thereof, operably linked to a control sequence permitting expression of the polypeptide in said cell line; <u>and wherein</u> the nucleic acid sequence <u>being</u> (i) <u>capable of complementing complements</u> the endogenous gene and (ii) <u>unable</u> to does not undergo homologous recombination with the endogenous gene;

- (b) isolating mutant HSV from the cultured cell line;
- (c) optionally purifying the mutant HSV; and
- (d) formulating the mutant HSV with a pharmaceutically acceptable carrier or diluent.

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Claim 2. (Cancelled)

- 3. (Currently Amended) A process according to claim 2 1 wherein the functional equivalent of the HSV VP16 homologue polypeptide is encoded by a herpes virus gene selected from a bovine herpes virus gene and an equine herpes virus gene.
- 4. (Original) A process according to claim 3 in which the herpes virus gene is equine herpes virus 1 gene 12, or the bovine herpes virus gene BTIF.
- (Original) A process according to claim 1 wherein the control sequence comprises a constitutively active promoter or an inducible promoter.

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Claim 6. (Cancelled)

- 7. (Currently Amended) A process according to claim 6 1 wherein the HSV is an HSV-1 or HSV-2.
 - 8. (Currently Amended) A process according to claim 1 wherein the mutant herpes simplex virus comprises additional mutations which functionally inactivate one or more additional endogenous genes of said virus and the cell line comprises additional nucleic acid sequences encoding functional herpes virus genes which complement said additional functionally inactive endogenous genes.
 - 9. (Currently Amended) A process according to claim 8 wherein said additional nucleic acid sequences encode at least one of HSV-1 ICP27 and/or, HSV-1

ICP4, or an equivalents of said HSV-1 ICP27 thereof in HSV-2 or another herpes virus and an equivalent of said HSV-1 ICP4 in HSV-2 or another herpesvirus.

of said HSV-1 ICP27 or said equivalent thereof is driven by the ICP27 promoter and/or in which and said HSV-1 ICP4 or equivalent thereof is driven by the MMTV LTR promoter.

Claims 11-26 (Cancelled)

- 27. (Currently Amended) A pharmaceutical composition obtained by a process according to claim 12 1.
- 28. (New) A process according to claim 1 wherein the mutant herpes simplex virus comprises a heterologous gene.
- 29. (New) A process according to claim 28 wherein the heterologous gene is operably linked to a control sequence permitting expression of the heterologous gene in a mammalian cell.
- 30. (New) A process according to claim 28 wherein said heterologous gene is an HSV gene that is not operably linked to the viral control sequence with which it is naturally associated.

- 31. (New) A process according to claim 28 wherein said heterologous gene encodes a polypeptide of therapeutic use.
- 32. (New) A process according to claim 9 wherein said additional nucleic acid sequences additionally encode HSV-1 ICP27 or an equivalent thereof in HSV-2 or another herpes virus.
- 33. (New) A process according to claim 32 wherein the HSV-1 ICP27 or equivalent thereof is driven by the ICP27 promoter.
- 34. (New) A process for propagating a mutant herpes simplex virus (HSV) comprising:
- (a) a mutation in its endogenous VP16 gene wherein the mutation reduces or abolishes the ability of the protein encoded by the VP16 gene to activate viral transcription without disrupting the structural activity of the protein; and
 - (b) a heterologous gene;

which process comprises infecting a cell line with the mutant herpes virus and culturing the cell line,

wherein the cell line comprises a nucleic acid sequence from a non-HSV herpes virus encoding a functional equivalent of the HSV VP16 polypeptide operably linked to a control sequence permitting expression of the polypeptide in said cell line and wherein

the nucleic acid sequence (i) complements the endogenous gene and (ii) does not undergo homologous recombination with the endogenous gene.

- 35. (New) A process according to claim 34 wherein the functional equivalent of the HSV VP16 polypeptide is encoded by a herpes virus gene selected from a bovine herpes virus gene and an equine herpes virus gene.
- 36. (New) A process according to claim 35 in which the herpes virus gene is equine virus gene is equine herpes virus 1 gene 12, or the bovine herpes virus gene BTIF.
- 37. (New) A process according to claim 34 wherein the control sequence comprises a constitutively active promoter or an inducible promoter.
- 38. (New) A process according to claim 34 wherein the HSV is an HSV-1 or HSV-2.
- 39. (New) A process according to claim 34 wherein the mutant herpes simplex virus comprises additional mutations which functionally inactivate one or more additional endogenous genes of said virus and the cell line comprises additional nucleic acid sequences encoding functional herpes virus genes which complement said additional functionally inactive endogenous genes.

- 40. (New) A process according to claim 39 wherein said additional nucleic acid sequences encode at least one of HSV-1 ICP27, HSV-1 ICP4, an equivalent of said HSV-1 ICP27 in HSV-2 or another herpes virus, and an equivalent of said HSV-1 ICP4 in HSV-2 or another herpes virus.
- 41. (New) A process according to claim 40 in which at least one of said HSV-1 ICP27 or said equivalent is driven by the ICP27 promoter and said HSV-1 ICP4 or equivalent is driven by the MMTV LTR promoter.
- 42. (New) A process according to claim 40 wherein said additional nucleic acid sequences additionally encode HSV-1 ICP27 or an equivalent thereof in HSV-2 or another herpes virus.
- 43. (New) A process according to claim 42 wherein the HSV-1 ICP27 or equivalent thereof is driven by the ICP27 promoter.
- 44. (New) A process according to claim 34 which the heterologous gene is operably linked to a control sequence permitting expression of the heterologous gene in a mammalian cell.
- 45. (New) A process according to claim 34 wherein the heterologous gene is an HSV gene that is not operably linked to the viral control sequence with which it is naturally associated.

- 46. (New) A process according to claim 34 wherein the heterologous gene encodes a polypeptide of therapeutic use.
- 47. (New) A process for propagating a mutant herpes simplex virus (HSV) having a mutation in its endogenous VP16 gene that reduces or abolishes the ability of the protein encoded by the VP16 gene to activate viral transcription without disrupting the structural activity of the protein, which process comprises infecting a cell line with the mutant herpes virus and culturing the cell line,

wherein the cell line comprises a nucleic acid sequence encoding a functional equine herpes virus (EHV) gene 12, operably linked to a control sequence permitting expression of the EHV gene 12 polypeptide in said cell line.

- 48. (New) A process according to claim 47 wherein the control sequence comprises a constitutively active promoter or an inducible promoter.
- 49. (New) A process according to claim 47 wherein the HSV is an HSV-1 or HSV-2.
- 50. (New) A process according to claim 47 wherein the HSV comprises additional mutations which functionally inactivate one or more additional endogenous genes of said virus and the cell line comprises additional nucleic acid sequences

encoding functional herpes virus genes which complement said additional functionally inactive endogenous genes.

- 51. (New) A process according to claim 50 wherein said additional nucleic acid sequences encode at least one of HSV-1 ICP27, HSV-1 ICP4, an equivalent of said HSV-1 ICP27 in HSV-2 or another herpes virus, and an equivalent of said HSV-1 ICP4 in HSV-2 or another herpes virus.
- 52. (New) A process according to claim 51 in which at least one of said HSV-1 ICP27 or said equivalent is driven by the ICP27 promoter and said HSV-1 ICP4 or equivalent is driven by the MMTV LTR promoter.
 - 53. (New) A process according to claim 51 wherein the additional nucleic acid sequences additionally encode HSV-1 ICP27, or an equivalent thereof in HSV-2.
 - 54. (New) A process according to claim 53 wherein the HSV-1 ICP27 or equivalent thereof is driven by the ICP27 promoter.
 - 55. (New) A process according to claim 47 wherein the mutant herpes simplex virus comprises a heterologous gene.

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- 56. (New) A process according to claim 55 wherein the heterologous gene is operably linked to a control sequence permitting expression of the heterologous gene in a mammalian cell.
- 57. (New) A process according to claim 55 wherein said heterologous gene is an HSV gene that is not operably linked to the viral control sequence with which it is naturally associated.

58. (New) A process according to claim 55 wherein said heterologous gene encodes a polypeptide of therapeutic use.